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FLEAS AND DISEASE[1]

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Introduction

In the broad field of disease caused by arthropod-borne agents there are many instances wherein the pathogenic organism appears to be well adapted to the vector and may even pass an essential part of its life cycle therein, as do the malaria parasites of man within the anopheline mosquitoes. The pathogen may be carried from stage to stage or even passed from one generation to another through the egg (transovarial passage). These adaptations of parasite to arthropod vector are thought to result from a long host-parasite association. The arthropod, in such instances, is conveniently referred to as a biologic vector of the pathogen.

In a few instances there is a closer relationship between vector and pathogen in which groups of related pathogens are transmitted by groups of related arthropods. Both pathogens and arthropods show about the same relative degree of diversity and homogeneity. Considerable host-parasite specificity is exhibited by both vector and parasite. An outstanding example of this degree of relationship is the relapsing-fever group of spirochetes of the genus *Borrelia* and their tick vectors of the genus *Ornithodoros*. Both are distributed in all the major faunal regions, in temperate and tropical zones, and occur in definite tick-spirochete combinations. These spirochetes exhibit a high degree of vector specificity, are maintained in part through transovarial passage, and develop in the body cavity of the tick. Only a single species is not carried by ticks, i.e., *Borrelia recurrentis* (Lebert), the cause of louse-borne relapsing fever of man.

The malarial parasites also fall in this category and are transmitted only by mosquitoes: human and other primate malaria by *Anopheles,* bird malaria by *Culex* and other genera. Transmission in nature is accomplished by no other means than the bite of mosquitoes.

The rickettsial diseases of man and animals are in general associated with ixodid ticks, but here there are more exceptions. The tick-borne rickettsiae are beautifully adapted to their vectors and are even maintained by transovarial passage, a phenomenon not well established for any pathogen of vertebrates, either virus, bacteria, or protozoan, carried by an insect.

There seems to be no better way to refer to an arthropod-pathogen combination within such groups than as an "evolutionary vector of the respec-

[1] The survey of the literature pertaining to this review was completed in June, 1958.

tive pathogen," meaning that vectors and pathogens evolved from an ancestral vector-pathogen combination. This interpretation is generally accepted for the parallelism that exists between vertebrates and some of their parasites, and it is especially well exemplified in the mammals and their ectoparasitic Anoplura, Mallophaga, and to some extent by their Siphonaptera (50, 121).

In regard to fleas, there are several instances in which they are well-adapted biologic vectors of a pathogen. The only indication of a role as "evolutionary vector" is in their relationship to the *Trypanosoma lewisi* group of trypanosomes. Some of these relationships will be mentioned in this introduction and discussed in greater detail in the individual disease sections.

Members of the genus *Pasteurella,* which includes the plague organism, *Pasteurella pestis* (Lehmann & Neumann), and the agent of tularemia, *Pasteurella tularensis* (McCoy & Chapin), constitute a group of bacteria highly pathogenic for birds and mammals. There is no indication that characteristic strains of *P. pestis* are related to any special species, genera, or families of fleas. While the organism is dependent upon fleas for its perpetuation and transmission, it does not invade the tissue of the flea, does not pass an essential part of its life cycle in the flea, and is frequently deleterious to the flea. There is much evidence that world-wide spread of plague has taken place within historic times. This would be interpreted as a poorly adapted biologic-vector relationship but not an evolutionary-vector relationship. The three other species of *Pasteurella* are not associated with insect transmission. Fleas have not been shown to be important vectors of tularemia, and the causative organism has definite biologic vectors, mainly among the ixodid ticks.

Murine typhus is the only rickettsial disease associated with fleas. Although most rickettsiae are carried by ticks and some by mites and lice, one (the agent of Q fever) may be quite independent of arthropod transmission. The organism of murine typhus is well adapted to flea transmission and multiplies intracellularly within the flea, where it is not noticeably harmful. There are no well-defined strains associated with certain genera of fleas, nor is there evidence to suggest the flea is more than a biologic vector.

Some mammalian trypanosomes are transmitted by tsetse flies, *Glossina,* and others by blood-sucking Hemiptera, *Triatoma* and related genera. However, there is the rather homogenous "*lewisi* group" that, with the exception of *Trypanosoma cruzi* Chagas, is carried by fleas. These pathogens parasitize a considerable variety of hosts in three orders, Rodentia, Insectivora, and Lagomorpha. The parasites invade flea cells, where they undergo a cyclic development, but they do not appear to be deleterious to the flea or to the natural mammalian hosts. Pathogen-vector-vertebrate associations are specific enough to suggest a long evolutionary relationship.

The relationship of fleas to plague, murine typhus, trypanosomiasis, and other diseases will be considered more thoroughly after a general discus-

sion of fleas themselves. We shall find that fleas probably are not the vectors of heart worm of dogs but may carry another dog filarid; that they are the alternate hosts for a dog tapeworm and two rodent tapeworms; that they may carry myxoma virus of rabbits, cause anemia, live in subcutaneous cysts, and inflict most grievous bites on man. It may be some consolation to learn that, in turn, fleas are parasitized by mites, nematodes, a chalcid fly, many protozoa, and are preyed upon by small beetles.

Fleas

In 1901, the Honorable N. Charles Rothschild, a banker of the House of Rothschild and a world authority on fleas, together with A. F. R. Wollaston, collected a number of fleas in Egypt and in the Sudan from various small mammals. At least five new species were represented in this collection. One of these was collected from *Acomys witherbyi* DeWinton, *Gerbillus robustus* (Cretzschmar), *Arvicanthis testicularis* Sundevall, *Dipodillus watersi* (DeWinton) *Dipus jaculus* (Linnaeus), and *Genetta dongolana* (Hemprich & Ehrenberg), all from Shendi. It was earlier collected from *Mus gentilis* Brants, near Suez, by Mr. W. E. DeWinton on October 17, 1900. This species was named *Pulex cheopis* when Rothschild described and figured it in 1903 (103). Little did these naturalists suspect that they were collecting and identifying one of the great insect panacides of all times, one which ranks with the yellow-fever mosquito, *Aedes aegypti* (Linnaeus), and the carrier of epidemic typhus, *Pediculus humanus* Linnaeus. The plague flea has also been known under the following names: *Pulex murinus* Tiraboschii, *Pulex philippinensis* Schultz & Herzog, *Xenopsylla pachyuromydis* Glinkiewicz, *Loemopsylla cheopis* Rothschild, and *Pulex tripolitanus* Fulmek. Today it is known as *Xenopsylla cheopis* (Rothschild).

Previous to the twentieth century, a rich literature on plague existed with contributions in poetry, fiction, history, and medical writings in several languages, a fine synopsis of which is given by Key's "The Plague in Literature" (62), with references dating from 430 B.C. to 1938. Fleas, on the contrary, do not have such a literary background prior to their definite association with plague about 1904.

In 1895, Baker (14) was able to list only 35 known species of fleas for the world, two of which had been described by Linnaeus in 1758. Baker assigned these to six genera and three families. By 1904 (15) he had catalogued 134 species and in the succeeding year added another 120 to the world list, many of these by his own descriptions. Holland (48) in a short synopsis of the history of Siphonaptera estimates there are now 1350 known species, divided among 200 genera.

The dramatic discovery that sylvatic plague was widespread in western United States in 1934 and 1935 and in Canada in 1939 was a great stimulus to flea studies in North America, and since that time many short papers and the following extensive and important works on fleas have appeared

in North American literature (32, 35, 47, 52, 56, 57, 110, 117). Prominent contributions to the world literature are papers of Uriarte (118), Costa Lima & Hathaway (66), Liu (69), Jameson (55), and Rosicky (101). The most ambitious venture in flea publications since the discontinuation of "Ectoparasites," [1915 to 1924 (60)] is the appearance of the *Catalogue of the Rothschild Collection of Fleas (Siphonaptera) in the British Museum,* which is edited by G. H. F. Hopkins & Miriam Rothschild (49). It is understood that eight volumes are planned for this catalogue, which is in reality a monograph of the fleas of the world. There are many publications on fleas, plague, and pertinent rodent ecology from the U.S.S.R. in both Russian and German literature [Ioff (53, 54)]. These are especially important to us because of the close taxonomic and ecologic relationship of Palearctic and Nearctic fauna, but this literature has not yet been integrated into our own studies.

Considerable literature exists on the origin of fleas and their affinity with other insects, much of which is referred to by Sharif (106). Agreement is lacking on these points but it can be said that the phylogeny of fleas has not been found in fossil records or in their own ontogeny. In parallel with other metazoan parasites, including insects, one would expect, except for the organs of reproduction, that evolution would be accompanied by a general simplification which would include reduction of the organs of locomotion (the wings are already obliterated except in the pupal stage) and reduction in ornamentation. In fleas, this would mean evolution from the large, ornate, nearly free-living, nest-inhabiting types, such as *Hystrichopsylla,* toward simplified, unornamented, fixed, cutaneous parasites with reduced thoracic segments, such as *Echidnophaga*; the evolution culminates, finally, in the fixed subcutaneous and almost spineless *Tunga.* In this view the writer is diametrically opposed to many competent workers, including Oudemans (90) and Sharif (106). Sharif states, ". . . this would tend to the conclusion that less hairy fleas without spines are more primitive." The subject is also discussed by Jordan (59). Proper orientation on this point would give much more meaning to flea taxonomy, which has already contributed much to the understanding of the biologic role of fleas in the transmission of disease agents.

Some attempts have been made to use fleas as an indicator of mammalian relationships. Related fleas are often found on related animals throughout the world. Most of the bat fleas belong to a single family whose members are not found on any other hosts. The rabbit fleas of Asia and of North America are related. The same is true of the ground-squirrel fleas. The thesis that flea phylogeny parallels host phylogeny has been discussed by Wagner (122) and has been more fully explored by Hopkins (51), who concludes ". . . the existing pattern is almost useless as a guide to the phylogeny of the hosts and almost never reliable for the chronology of the associations."

Plague

The plague bacillus is carried by fleas. . . . If this simple fact had been known in the twelfth century, the history of Europe and its colonies would have been different. What the difference would have been is difficult to imagine, but plague probably retarded western civilization by 200 years. Establishment of flea transmission depended upon development of the microscope, the beginning of a science of bacteriology, identification of the plague organism in man and rats, the formation of a hypothesis of plague transmission by fleas, and final experimental proof of the hypothesis. The discovery of the plague organism did not impose any special technical difficulty, but many other important pathogenic bacteria were discovered in a relatively short period of time just before the plague organism was described. The reason for this is that plague was not then present in Europe, the center of bacteriological science.

As the discovery of the role of fleas in the transmission of plague is inseparably linked to identification of the organism, it seems well to review that part of plague history in detail. The plague organism multiplied unseen, and perhaps unlooked for, in all the centuries of human history prior to 1894, and today it is not certain which of two men first discovered—within an interval of a few days—the etiological agent. The distinction must be assigned to either A. Yersin, a Dane, or S. Kitasato, a Japanese, or must be shared by them. Lagrange (64), who was at one time an assistant to Dr. Yersin in Indochina, has fairly presented the facts regarding the controversy over the discovery of the plague bacillus. The Hong Kong newspapers on June 14, 1894, announced that Kitasato had discovered an organism which he thought caused plague. His claim was challenged on the basis that some of his preparations were made from a corpse 11 hours after death, that his description did not fit the plague organism, and that he denied that his organism was the same as that described by Yersin. On June 20, Yersin wrote that he saw "very small rods, thick with rounded ends, and lightly colored (Löfflers blue)" in preparations from a bubo, and further ". . . my bacillus is probably that of plague but I am not certain." Yersin's description is consistent with characters of plague bacilli, and this description has enabled others to recognize the pathogens, insofar as is possible, from morphology alone.

Lagrange states, "In 1925, as chairman of the Congress of the Far Eastern Medical Association, before 400 members, amongst whom were 250 foreign delegates, Kitasato is to be honored for having publicly stated that Yersin alone was the discoverer of the plague bacillus." Both men had already established their status as bacteriologists of their period. Yersin had collaborated with Roux on the study of diphtheria and its toxin. Kitasato had cultured the bacillus of tetanus for the first time. The flames of nationalism have kept this controversy alive, although the principals long ago considered it settled. Perhaps we should give Kitasato more credit than

he gave himself in this moment of magnanimity and concede that he first saw the bacillus and that Yersin first described it accurately.

One of the first important developments following identification and culture of *Pasteurella pestis* by Yersin and by Kitasato was the final establishment that rat plague and human plague were caused by the same organism. The relation of rat epizootics to human epidemics had been observed since antiquity, the rat epizootic usually preceding the human cases.

Persistence and prevalence of plague in India after its subsidence in many other countries invited, if not demanded, action from the scientific world, and in 1904 steps were taken in England to organize an advisory committee and a working commission, later known as the "India Plague Commission," to inquire into the problem. Results of this inquiry appear in the literature as *Reports on Plague Investigations in India,* usually without identification of specific scientists. The work of the Commission was so important that it seems fitting to name the early members, who were: Charles Martin, George Lamb, William Glen Liston, George Ford Petrie, Sydney Rowland, Thomas Henry Gloster, M. Kasava Pai, V. L. Manker, P. S. Ramachandrier, and C. R. Arvi. No doubt personnel of the Commission changed as work progressed.

A historical review on insect transmission of plague was prepared by the Advisory Committee of the India Plague Commission and published (1) as an introduction to the reports of their own experimental work. The Committee gave generous credit to many investigators for contributions leading to the conclusion that the plague bacillus is transmitted by fleas. Yersin (131), Hankin (43), and Nuttall (87) found virulent plague bacilli in dejecta of flies and ants that fed on infected organs. Nuttall fed bugs (presumably bed bugs) on infected mice and found that they harbored the bacilli but did not transmit them by bite. Ogata (88) injected crushed fleas from rats dead of plague into two mice, one of which died of plague after three days. He suggested, from epidemiological considerations, that plague was conveyed mostly by suctorial insects such as mosquitoes and fleas.

Simond (109) found organisms morphologically indistinguishable from plague bacilli in the stomach of fleas which had fed upon rats and mice dying of plague, and he succeeded in infecting a mouse by injecting an extract of crushed fleas taken from a plague rat. He found that in the absence of fleas plague was not transmitted from sick or dead rats to healthy rats in close proximity, but in at least two instances he observed transmission when fleas were present. He conjectured (wrongly) that the actual mode of transmission was by contamination of the skin with infected flea feces at the site of bite.

On purely epidemiological grounds based on observations of plague in Sidney, Australia, Thompson (116) arrived at a "theory of plague" that involved or necessitated transmission by fleas. Gauthier & Raybaud (39) repeated Simond's experiments and were able to transmit infection by fleas from rat to rat at least five times. Probably at least some of their fleas

were *Xenopsylla cheopis* (Rothschild). Liston (68) found that guinea pigs exposed in plague houses in Bombay became infested with rat fleas and then died of plague.

Other contemporary investigators in the early part of the century experienced conflicting results and some discounted the role of fleas as vectors of plague. Their results and views are more understandable now that the taxonomy and biology of fleas are better known, both because some fleas have proved to be very inefficient vectors, or show little tendency to bite man, and because of susceptibility of some hosts and resistance of others to plague infection.

The early work of the Commission (1) seemed well oriented by the findings of Yersin and Kitasato and by the experimental results of Simond and of Gauthier & Raybaud. The ingenuity, emphasized by simplicity, of their experiments led to the following results and conclusions, which with some refinements have been universally accepted. (*a*) "The presumption that plague was transferred from sick to healthy rats by the agency of fleas." This was based on 30 positive transfers out of 50 completed attempts. (*b*) "The possibility of the rat flea, *X. cheopis,* carrying plague from one rat to another is therefore demonstrated directly." This was based on 21 positive transfers out of 38 completed experiments in which normal animals had no other exposure to plague than fleas from known infected hosts.

After these basic issues were settled, the India Plague Commission advanced to other studies, including anatomy of the rat flea and "the mechanism by which the flea infects a healthy animal" (2). The workers determined that plague bacilli multiply in the stomach of a flea and that infection could result from the bite of a single flea. They could not find bacilli in body cavity or salivary glands and concluded, "No evidence has been obtained in favor of infection by contaminated mouth parts or regurgitation from the stomach, but the possibility of infection by such means cannot be excluded." They had studied the internal anatomy of fleas and were familiar with the function of the proventriculus. They followed development and multiplication of plague bacilli in the flea stomach and seriously considered the possibility of infection by regurgitation. It seems to this writer that they should have been rewarded by the ultimate discovery of how plague is transmitted by fleas.

The fine point of infection by regurgitation remained obscure until 1914, when it was elucidated at the Lister Institute in England by Bacot & Martin (11), and presented in a brief but historically important paper from which I quote:

> In a proportion of infected fleas the development of the bacilli was found to take place to such an extent as to occlude the alimentary canal at the entrance to the stomach. The culture of pest appears to start in the intercellular recesses of the proventriculus, and grows so abundantly as to choke this organ and extend into the oesophagus. Fleas in this condition are not prevented from sucking blood as the pump is in the pharynx, but they only succeed in distending an already contami-

nated oesophagus, and, on the cessation of the pumping act, some of the blood is forced back into the wound. Such fleas are persistent in their endeavours to feed, and this renders them particularly dangerous. Fleas suffering from obstruction do not necessarily perish, and in the course of some days the culture obliterating the lumen of the proventriculus may autolyse and passage again become pervious.

This discovery did much to clarify the role of fleas in the transmission of plague and to harmonize the conflicting results of many previous experiments and experimenters.

After plague appeared in Hong Kong and Canton in 1894, it spread rapidly to other coastal cities of the world. In 1899, there were at least three instances of plague on ships entering United States ports (67). It is not likely that plague became established in our ports from any of these ships. However, on March 6, 1900, plague was diagnosed in a Chinese resident in San Francisco. Sporadic cases occurred there throughout the summer and fall, and diagnosis of these cases stirred up a controversy that swept through newspapers, political and medical circles, and even into the courts, which attempted to establish by judicial pronouncement that plague was not present in San Francisco. The story is well told by Kellogg (61) and should be read in its entirety. Some measure of the emotions aroused are indicated in his statement:

> They [newspapers] launched a campaign of vilification against the Health Board and the Federal Quarantine Officer, Dr. Kinyoun, that for unexampled bitterness, unfair and dishonest methods, probably never had been and never again will be equalled.

At the request of Surgeon J. H. White of the United States Marine Hospital Service (forerunner of the United States Public Health Service), the Secretary of Treasury, L. J. Gage, appointed a committee of prominent bacteriologists to settle the question. This committee consisted of Professors Simon Flexner of the University of Pennsylvania, F. G. Novy of the University of Michigan, and L. F. Barker of the University of Chicago. In spite of the efforts of the governor of California, some members of the legislature and the president of the University of California to block their work, they found plague present in San Francisco. The toll of plague in this first epidemic for San Francisco, ending in 1904, was recorded as 121 cases and 118 deaths.

Plague reappeared in San Francisco in 1907 and occurred in Seattle the same year, in New Orleans in 1912, in other Gulf Coast cities in 1920, and in Los Angeles in 1924. Vigorous rat- and flea-control measures have eliminated it from our cities insofar as can be determined, but plague still persists in wild rodent populations (sylvatic plague).

The more serious aspects of sylvatic plague are a matter of record. The disastrous pneumonic plague epidemics that ravaged Manchuria in 1910 and 1911 and in 1920 and 1921 started among hunters and trappers who were taking marmots, *Marmota bobac* Pallas. The toll of the former epidemic was estimated at 60,000 and of the latter at 9300 victims. Since then the suspi-

cion has been entertained that sylvatic infection has a greater tendency to induce pneumonia than rat plague and therefore to become highly contagious (79).

The discovery in 1908, by the United States Public Health Service, that plague in North America was no longer confined to rats and rat fleas but had become established in ground squirrels, *Citellus beecheyi* (Richardson) in Contra Costa County, California, was an incentive for a new line of study on taxonomy, biology, disease, and control of both native rodents and their flea parasites. (An unexpected development from this study was the discovery of a new disease, tularemia, in Tulare County, California, where it was first known as a "plague-like disease of rodents.") This work was further stimulated when plague was found in native rodents in Modoc County of northern California [1934], then in Oregon [1935], in Montana east of the Continental Divide [1935], and in Alberta, Canada [1939]. A systematic survey of rodents and rodent fleas for plague which was already in progress was greatly intensified and its range extended. Most of the state health departments in the West cooperated with the United States Public Health Service Laboratory in San Francisco in this survey and plague was found to be endemic in 14 western states and two Canadian provinces, Alberta and Saskatchewan. It was found in 38 species and subspecies of rodents and lagomorphs. The Sciuridae or squirrel family were most prominent carriers [Meyer (78)]. Over 4000 isolations of plague were made [Link (67)]. This type of plague has come to be known as sylvatic or campestral plague and is present in many parts of the world.

As to the future of plague, I should like to quote from Pollitzer (96):

> However, even though plague, which but a few decades ago ranked high among the diseases decimating mankind, now occupies a rather inconspicuous place in the fatality lists, it would be wrong to assume that this infection has altogether lost its sting.

The last chapter on plague has not been written, but a measure of its present status is given in *Time* (9), which states:

> The World Health Organization announced in Geneva that in 1957 only 514 deaths due to plague were reported in the free world and only 44 of them in India. At long last, it looked as though the Black Death was licked.

The work of the India Plague Commission, the Manchurian Plague Commission, the microbiologists and entomologists in U.S.S.R. and in the U. S. Public Health Service, and of thousands of unnamed rat catchers has contributed to this achievement.

Practical world-wide control of the unholy trinity, *Rattus rattus, Xenopsylla cheopis,* and *Pasteurella pestis* is a *fait accompli.*

Tularemia

Pasteurella tularensis (McCoy & Chapin), the etiologic agent of tularemia, has many vertebrate reservoirs and arthropod vectors in nature and

other potential vectors that have been implicated by laboratory experiment only. Ticks are especially efficient vectors and often carry the bacterium to man. In some ticks the organism passes transovarially as well as from larva to nymph to adult. Deer flies of one species only, *Chrysops discalis* Williston, are important carriers of infection to man in the western United States.

The first scientific paper on tularemia [McCoy (73)] reported recovery of infection from fleas, *Diamanus montanus* (Baker) (=*Ceratophyllus acutus* Baker), taken from a sick or dead ground squirrel and tested in guinea pigs. McCoy attempted to transmit the disease by placing healthy animals in cages with flea-infested sick squirrels. In several experiments, transmission was effected, but in one experiment presence of buboes in the cervical region suggested transfer by ingestion rather than by flea bite.

Transmission of *P. tularensis* from sick to healthy water rats by fleas, *Megabothris walkeri* (Rothschild), is recorded by Olsufiev (89), who also reported: recovery of infection from *Ctenophthalmus assimilis* (Taschenberg) and *Ctenophthalmus pollex* Wagner & Ioff in nature; persistence of infection for four months in *Neopsylla setosa* Wagner; and laboratory transmission with *C. assimilis, Ctenophthalmus agyrtes* (Heller), *Amphipsylla rossica* Wagner, and *Ctenopsylla segnis* (Schönherr). He did not consider fleas efficient vectors.

In one report of the Minnesota Wildlife Disease Investigation, Green, Evans, Bell & Larson (41) recorded the recovery of *P. tularensis* from one lot of four fleas removed from a snowshoe rabbit, *Lepus americanus* Erxleben, and from three lots of one, nine, and three fleas, respectively, from cottontail rabbits, *Sylvilagus floridanus* (Allen). All were tested by animal inoculation. In no instance was infection recovered from fleas when it was not demonstrated in the host, either snowshoe hare or cottontail. The fleas concerned in these tests are referred to as "*Spilopsyllus cuniculi* (Dale)," which is the European rabbit flea, whereas the common fleas on snowshoe hares are *Hoplopsyllus glacialis lynx* (Baker) and the characteristic fleas on cottontails in Minnesota are *Cediopsylla simplex* (Baker) and *Odontopsyllus multispinosus* (Baker). Waller (123) later recovered *P. tularensis* from fleas, *C. simplex,* taken from a sick cottontail rabbit in Iowa.

Tularemia infection is very infrequently recovered when wild-rodent fleas are tested for plague at the San Francisco Laboratory. These findings are usually announced in the Public Health Reports without authorship. One such report deals with recovery of infection from fleas of prairie dogs, *Cynomys leucurus leucurus* Merriam, collected in Wyoming (5) and another with fleas from ground squirrels in Alberta, Canada (6).

Prince & McMahon (99) found that *P. tularensis* persisted as long as 32 days in *Xenopsylla cheopis* (Rothschild) although neither this species nor *Diamanus montanus* (Baker) transmitted infection by bite. They also found that rabbit fleas (*Cediopsylla*) became infected with tularemia, but their transmission experiments were limited and unsuccessful.

There is very little or nothing in the epidemiology of tularemia in man to

suggest that fleas are important vectors (*37*). However, human infection is not a good indicator of the role of fleas as vectors among wild rodents because wild-rodent fleas do not have the intimate contact with man or the predilection to bite him that rat fleas have. It is possible that fleas are more important in the spread of tularemia in rabbits and rodents than is now recognized, and the subject invites further investigation.

Salmonellosis

The transmission of *Salmonella enteritidis* (Gaertner) by *Pulex irritans* (Linnaeus) and *Ctenocephalides canis* (Curtis) was studied by Varela & Olarte (119). They found that the pathogens survived in fleas up to 96 hours, but transmission by bite was not demonstrated.

In the course of laboratory investigations on plague, Eskey, Prince & Fuller (31) found that some of their fleas had become accidentally infected with *S. enteritidis*. They then demonstrated that *X. cheopis* and *Nosopsyllus fasciatus* (Bosc) could transmit the infection to mice. The exact mode of transmission was not determined, but regurgitation into the bite wound seemed probable. Large numbers of organisms were found in flea feces, and in some instances excessive defecation indicated that the infection was deleterious to the flea. The same flea species were also infected with *Salmonella typhimurium* (Loeffler) but did not transmit infection to mice.

Murine Typhus

Fleas are generally accepted to be the vectors of murine typhus, also known as endemic typhus, flea-borne typhus, Mexican typhus (in part), and tabardillo. The name "Brill's disease" has been applied to this entity but in a strict sense it is not appropriate; the reasons will be discussed later. The causative organism of flea-borne typhus is *Rickettsia (Rickettsia) typhi* (Wolbach & Todd). For a discussion of the nomenclature of this organism the reader is referred to Mooser (81) and Philip (92).

The evidence that fleas are the only vector or even the principal vector of the rickettsia of murine typhus is not conclusive, and the exact method of transmission has not been established. Transmission may be by flea or mite bite, by passage of infection through the skin where it has been abraded by scratching flea bites and contaminated by infected flea feces, by inhalation or ingestion of rickettsia-laden flea feces or rickettsia-laden rodent urine in the dust of buildings. All methods may be effective at one time or another.

The significant steps in the identification of murine typhus as a disease entity, distinct from epidemic typhus, and studies on probable arthropod vectors of murine typhus are deserving of review. Dyer (*27*) states that epidemic typhus was brought to Canada in 1659 and that over 20,000 deaths from typhus occurred among Irish immigrants in Canada about 1847. It is accepted that epidemic louse-borne typhus was prevalent in eastern North America at one time but probably died out before 1900. Brill (18) recognized a typhuslike disease which he could not accept as epidemic typhus and

in a publication which is a classic in medical science recorded 221 cases. Most of the cases were in New York City. This entity or complex of diseases has been designated correctly as "Brill's disease," but its full significance was not realized until careful epidemiologic and laboratory work identified at least three distinct kinds of typhuslike disease in the Eastern Seaboard states, namely, recrudescent epidemic typhus, flea-borne typhus, and spotted fever. Two other rickettsial diseases, rickettsialpox and Q fever, are present in the area, but have little or no clinical resemblance to the typhus fevers.

Although many writers have referred to the murine or flea-borne typhus of the southeastern states as "Brill's disease," on the basis of presently known geographic distribution it is quite likely that Brill in New York City was dealing exclusively with recrudescent epidemic typhus, and, therefore, the name "Brill's disease" is not applicable to murine typhus. "Brill's disease," which we considered to be a distinct entity, was shown by Zinsser (132) and Plotz, Wertman & Bennett (93) to be a long-delayed recrudescence of Old World typhus, usually in immigrants, caused by the organism *Rickettsia prowazeki* da Rocha Lima, and mainly confined to the large eastern cities.

Another typhuslike disease was identified in the Eastern Coastal states in 1932 when Badger (12) isolated the rickettsia of spotted fever, *Rickettsia* (*Dermacentroxenus*) *rickettsii* (Wolbach, 1919) from ticks, *Dermacentor variabilis* (Say). Spotted fever has since been found widespread with many important endemic foci in the eastern states. Certainly, prior to 1932, some cases of spotted fever were diagnosed as "Brill's disease" or murine typhus.

Paullin (91) in Georgia, where murine typhus is now known to be common, was among the first to recognize a clinical typhus fever without mortality, thus distinct from classical typhus. Neill (84) observed that certain strains of Mexican typhus produced orchitis in a large proportion of experimental male guinea pigs and that swelling was suggestive of spotted fever rather than European typhus. Mooser (80) confirmed this finding and interpreted it as a "biological difference" between the two types of typhus. Much work was done on typhus fevers in Mexico, but in published reports it is difficult or impossible to tell just when workers were dealing with flea-borne typhus and when with epidemic typhus. Both forms were present and both were referred to as tabardillo or Mexican typhus.

After a careful epidemiologic study, Maxcy (77) postulated the necessity of a rodent reservoir and insect vector for typhus in the eastern states. It remained for Dyer, Rumreich & Badger (29) to make the first isolation of murine typhus from rat fleas collected at a typhus focus in Baltimore. Dyer, Ceder, Rumreich & Badger (28) later showed that the organisms of murine typhus persisted in rat fleas for at least nine days and were present in feces of infected fleas. They were also successful in experimental transmission of murine typhus from rat to rat with *X. cheopis*.

Studies on multiplication of the rickettsia in fleas were done by Dyer, Workman, Ceder, Badger & Rumreich (30) and by Mooser & Castañeda (82).

The former authors found that in rat fleas, *X. cheopis,* fed on infected animals the agent passed an incubation period of two or three days and the fleas became highly infectious on the fifth or sixth day. In three instances, an inoculum representing "1/128,000th of a flea" produced infection. This was the highest dilution tested. Fleas remained infectious for 40 days and presumably for life without evidence of ill effect. Mooser & Castañeda (82) followed, by cytologic methods, the development and multiplication of the rickettsia of murine typhus in tissues of several species of fleas, including *X. cheopis, Nosopsyllus fasciatus* (Bosc), *Leptopsylla musculi* (Duges), *Ctenocephalides canis* (Curtis), *and Ctenocephalides felis* (Bouche). They found that the rickettsia multiplied abundantly in epithelial cells of the stomach, but that the organisms were prevented by the peritrophic membrane from entering the lumen of the gut in quantity. Multiplication also took place in cells of the malpighian tubules and these cells were probably the source of organisms found in the lumen of the gut and feces. They considered fleas to be relatively inefficient vectors of typhus.

Early workers on murine typhus were disappointed in the vector efficiency of fleas, for they found that when experimental hosts were carefully protected from contamination with flea feces, infection was not transmitted by feeding alone. However, when feces from infected fleas were rubbed into abraded skin, as would occur when flea bites were scratched, infection resulted [Ceder, Dyer, Rumreich & Badger (20)].

Serious doubt as to the exclusive role of fleas in transmission of endemic typhus was first introduced by Dove & Shelmire (24, 25), following their laboratory studies with the tropical rat mite, *Ornithonyssus bacoti* (Hirst) (=*Liponyssus bacoti*). They were able to transmit the disease from guinea pig to guinea pig and from guinea pig to rat with these mites. They demonstrated transovarial passage of the organism in mites. This cosmopolitan mite frequently bites man and is sometimes abundant. Contemporary critics [see (24) for abstracts of discussion] expressed some skepticism that Dove & Shelmire were actually working with a strain of endemic typhus, but this criticism has not persisted.

Mooser, Castañeda & Zinsser (83) found that the rat louse was readily infected with murine typhus and transmitted the disease from rat to rat under simulated natural conditions. While it may be important, as they suggest, in maintaining enzootic infection, this louse does not bite man and would not be a direct cause of human infection. In order to clarify the rather confused vector relationships in endemic typhus, research workers then turned to extensive ecologic and epidemologic studies. Such studies have been reported by Rumreich & Koepke (104) for Florida, Alabama, and Honolulu and by Fox (36) for Puerto Rico. Their reports indicate that a tick and mites may be of some importance as vectors but they do not challenge seriously the theory that fleas are the principal carriers to man.

A more extensive review of arthropods as vectors of endemic typhus was prepared by Kohls (63). It is now accepted that rat fleas of several species

play a prominent part as vectors of this disease. For a very extensive list of references on murine typhus, the reader is referred to *Bibliography on Epidemic, Endemic, and Scrub Typhus Fever* (7).

From about 1913, when "endemic typhus" was first recognized in the southern states, to 1945 there was a rapid rise in the number of cases reported for each consecutive five-year period, increasing from 199 in 1916 to 1920 to 21,572 in 1941 to 1945 [Andrews & Link (4)]. No doubt most of the increase may be attributed to "heightened awareness of the disease, improved diagnostic facilities, and more adequate case reporting on the part of attending physicians," as Andrews & Link state. The marked increase from 1936 to 1940 (11,299 cases), when the disease had become well known, to 1941 to 1945 (21,572 cases) strongly suggested increased prevalence in old areas and extension of infection into new localities. This rapid rise in case incidence prompted a vigorous campaign of research and control by the several states and the Public Health Service. The recorded case incidence reached a peak in 1944 with 5401 cases. In 1945 the incidence dropped slightly to 5193 cases and then rapidly declined for seven consecutive years to 186 cases for 1952, the last year for which figures are given by Pratt & Good (98). No doubt many of the measures applied in this widespread murine-typhus control program contributed to this decline, but Pratt (97) and Pratt & Good (98) give much credit to the general use of DDT dust, both as a rodenticide and as an insecticide.

Dyer (26) found three kinds of native wild rodents in the eastern United States susceptible to infection with endemic typhus. These were the woodchuck, *Marmota monax monax* (Linnaeus); the meadow mouse, *Microtus pennsylvanicus pennsylvanicus* (Ord); and the white-footed mouse, *Peromyscus leucopus noveborascensis* (Fischer). The introduced house mouse, *Mus musculus* Linnaeus, was also found to be susceptible. Indigenous rodents do not seem to be important as reservoirs of endemic typhus, in contrast to rats and mice of the introduced family Muridae in North America.

Woodward (128) states that, as a result of nearly world-wide search for disease agents stimulated by World War II, murine typhus is now known to be prevalent in North Africa, the West Indies, South America, the Philippines, and in all European and Asiatic countries.

Ioff (54) mentions a typhus of spermophiles, genus *Citellus,* in Russia that may be distinct from the well-known murine typhus. If this is the case, it is an extremely interesting discovery.

As facts from nature, the hospital, and the laboratory become known regarding a widespread disease, its epidemiology increases in complexity until it is no longer safe to make any positive, unqualified statement about it. Perhaps the best we can say in summary is that endemic typhus is a distinct entity but closely related to, and possibly derived from or progenitor to, classical epidemic typhus (13). It is primarily a disease of murine rodents, which include only the introduced rats, genus *Rattus,* and mice, *M. musculus,* in North America. It is spread from rodent to rodent by their fleas, lice, and possibly mites, and occasionally to man from rats and mice, presumably by

fleas. The most likely mode of infection is by organisms penetrating abraded skin at the site of flea bites contaminated by flea feces. Infection by direct bite remains a possibility, and infection by inhalation and ingestion is probable.

Murine typhus has practically disappeared from many large cities and has experienced a dramatic drop in incidence throughout the United States coincidental with vigorous control measures based on the premises outlined above.

Myxomatosis

Myxomatosis is a virus disease of wild and domestic rabbits and was first found in a native rabbit, *Sylvilagus braziliensis* (Linnaeus), in Brazil. It is transmitted by a great variety of blood-sucking insects but mosquitoes appear to be the most effective vectors (120). Aragão (10) and Day (22) studied transmission with *Ctenocephalides felis* (Bouche), which was able to transmit the virus but was not as efficient as three species of mosquitoes used in one experiment (22). Ratcliffe (100) stated:

> Circumstantial evidence has suggested transmission by the cat flea in one outbreak in northern New South Wales in 1952; but against this we have to record the failure of the infection to spread in rabbit populations infested with stick-fast fleas
> tion.

Bull & Mules (19) also worked with a stickfast flea, *Echidnophaga myrmecobii* Rothschild, and found it was not an efficient vector. Day (22) states, "It is regrettable that no work has been published on the mechanism of transmission by the rabbit flea, *Spilopsyllus,* which many English workers consider has been mainly responsible for the spread of the disease in Britain."

This deficiency has been in part corrected by Lockley (70) who succeeded in transmitting myxoma virus in seven of 10 attempts with the European rabbit flea, *Spilopsyllus cuniculi* (Dale).

It seems logical that some of the true rabbit fleas, *Spilopsyllus, Hoplopsyllus, Cediopsyllus,* or *Odontopsyllus,* would be more efficient vectors of a rabbit disease than *Echidnophaga,* which is not a specific rabbit parasite and has the added disadvantage of restricted mobility.

Myxomatosis has been introduced with considerable success into Australia for control of the European rabbit. It has also caused extensive and much publicized epidemics in wild rabbits in Europe and Great Britain since 1953. Under natural conditions the virus does not appear to spread to animals other than lagomorphs.

Trypanosomiasis

Fleas are vectors of certain trypanosomes, including *Trypanosoma lewisi* (Kent), of small mammals. This particular group of trypanosomes is considered to be nonpathogenic, in contrast to the virulent African species. Taliaferro (115) says that rodent trypanosomes ". . . are morphologically

identical or similar to *T. lewisi* of the rat, and are differentiated almost entirely by their specificity for their rodent hosts." A good account of *T. lewisi* and related forms is given by Wenyon (126). Hoare (46) places *Trypanosoma cruzi* in the "*lewisi* group." *T. cruzi* is the cause of Chagas's disease but is carried by *Triatoma* and related genera of Hemiptera. *T. lewisi* has been a classical organism for laboratory study and demonstration because of the ease with which it is maintained. It has been useful in the study of trypanosome life history and in immunology and therapy of trypanosomiasis.

T. lewisi multiplies in both mammalian host and flea vector. Organisms in the blood are taken up by the flea and may multiply in the lumen of the gut. However, some penetrate and multiply within the cells lining the stomach. Organisms re-enter the stomach by rupture of cells and are passed in flea feces. Organisms in various stages of development are found in fresh feces and are infectious when ingested by rats. Ingestion of infected fleas would be equally infectious. There is general agreement that this is the usual mode of rat infection, although one worker, Yamasaki (130), claimed that the dog flea can transmit trypanosomes by its proboscis. Transmission by other ectoparasites, including the rat louse, has been studied.

Insofar as other species of this group have been tested, they have been found to be transmissible by fleas, for example, *Trypanosoma duttoni* Thiroux of the mouse by a bird flea *Ceratophyllus hirudinis* Curtis; *Trypanosoma rabinowitschi* Brumpt of the hamster by *Typhlopsyllus assimilis* and *N. fasciatus;* and *Trypanosoma nabiasi* Ralliet of the rabbit by *Spilopsyllus cuniculi.*

The life cycle of the rabbit trypanosome, *Trypanosoma nabiasi,* in the rabbit and in the flea, *S. cuniculi,* has been determined by Grewal (42) who found that the parasite multiplies in the spleen of the rabbit and in the gut of the flea.

Several species of trypanosomes are present in some indigenous North American rodents, lagomorphs, and insectivores outside the known range of any *Triatoma* or related genera, and we may assume that they are transmitted by fleas. These *Trypanosoma* include *T. leporis-sylvaticus* Watson, *T. peromysci* Watson, *T. citelli* Watson, *T. evotomys* Hadwen, and *T. soricis* Hadwen of Canada (125), and *T. parkeri* Dias (23) from the marmot in Montana. *T. neotomae* Wood is present in wood rats, *Neotoma* spp., and in wood-rat fleas in California (127). The flea vector was given by Wood (127) as *Orchopeas wickhami* (Baker), which is a tree-squirrel flea, but it is more likely one of the many subspecies of *Orchopeas sexdentatus* (Baker) which are characteristic wood-rat parasites.

With the exception of *T. cruzi,* a species transmitted by Hemiptera, none of the rodent trypanosomes is known to be pathogenic for man. Fleas may be suspected as vectors of trypanosomes of birds in the northern part of our continent, although Herman (44) thinks that mosquitoes may be carriers. Bishopp (16) stated that the dog flea and human flea were suspected of car-

rying leishmaniasis in the Mediterranean region but other arthropods, *Phlebotomus,* have now been identified with this disease.

Some parasitic flagellates of fleas are occasionally mistaken for developing stages of mammalian trypanosomes.

Only in the trypanosomes do we have a group of related organisms transmitted by fleas. This host-parasite-vector association suggests a long evolutionary relationship.

Filariasis and Other Nematode Infestations[2]

Both mosquitoes and fleas have been considered as possible vectors of heart worm of dogs, *Dirofilaria immitis* (Leidy), because developmental stages have been found in them. In Australia, Breinl (17) found filarial larvae which he thought were *D. immitis* in fleas, *Ctenocephalides canis* and *Ctenocephalides felis.* Summers (114), in New Orleans, found many infected fleas, *C. canis, C. felis,* and *Pulex irritans,* on dogs and concluded: "It appears both biologically and epidemiologically fleas are more suitable intermediate hosts of *D. immitis* than had been previously supposed."

The role of fleas in relation to *D. immitis* transmission has recently been questioned by Newton & Wright (86) whose work "may shed light on some of the apparent discrepancies and unexplained findings reported for the dog heart worm." They have determined the existence of at least two types of microfilariae common in North American dogs. One is associated with adult heart worms, *D. immitis,* and develops in mosquitoes, *Anopheles quadrimaculatus* Say. In later experiments, Newton (85) reported the transmission of *D. immitis* by bite of *A. quadrimaculatus.* The other, probably the larva of *Dipetalonema reconditum* (Grassi), which is a parasite in subcutaneous tissues, develops in fleas, *C. canis* and *C. felis,* but fails to develop in mosquitoes. Successful transmission experiments with *D. reconditum* have not been reported.

In taxonomic flea studies, the writer has occasionally noted nematodes within the bodies of rodent fleas. Alicata (3) reported spirurid larvae in *C. felis* in Nebraska and cited a reference to spirurid larvae in *X. cheopis* and *N. fasciatus* in Australia. Sassuchin, Ioff & Tiflow (105) figure an adult nematode, *Neonema ctenophthalmi,* from *Ctenophthalmus pollex* and list other records of parasitism of fleas by nematodes.

Cestode Infestations

The cysticercoid stages of several tapeworms develop in fleas. One is the common cat and dog parasite, *Dipylidium caninum* (Linnaeus). Its immature stages have been found in *C. canis, C. felis, and P. irritans.* The life

[2] Since the preparation of this manuscript, the writer has received a relevant study: L. Kartman, "The Vector of Canine Filariasis; A Review With Special Reference to Factors Influencing Susceptibility," *Rev. brasil. malariol. e doenças trop.,* **8**(5), 1–41 (1957)

cycle was partly determined by Grassi & Rovelli (40). The mouth parts of an adult flea are not adapted to ingest a large tapeworm egg and this part of the cycle remained in doubt until Joyeux (58) showed that fleas become infected as larvae and that the cysticercoids remain viable and infective in the adult flea after metamorphosis. *D. caninum* is of medical importance, as it occasionally infests children. A closely related species, *Dipylidium sexcoronatum* von Ratz, develops cysticercoids in the biting louse of dogs, *Trichodectes canis* DeGeer. Stewart (111) has shown that physiological differences in respect to chemotherapy also exist between the two species, whose confusion has no doubt caused much difficulty in earlier life-cycle studies.

Some authors would greatly reduce the number of species in the genus *Dipylidium,* but Wardle & McLeod (124) list 20 species and provide a key to 13 species which were recognized by Lopez-Neyra (71). The life cycles of most of these have not been determined, but one may suspect that fleas are involved as hosts to other species besides *D. caninum.*

Wardle & McLeod (124) also list the following fleas as intermediate hosts of rodent tapeworms; *X. cheopis, C. canis,* and *P. irritans* for *Hymenolepis nana* Siebold; *Nosopsyllus fasciatus* (Bosc), and *X. cheopis* for *Hymenolepis diminuta* Rudolphi. These two cestodes have many other insect hosts, especially beetles. Although they are essentially rodent parasites, they frequently infest children.

Anemia

An anemia caused by excessive numbers of fleas, *C. canis,* on fox pups on a fur farm is described by Law & Kennedy (65). Red-blood-cell counts as low as 2,600,000 were observed after an infestation period of 15 days, whereas the normal count was about 7 million. When the fleas were removed, the animals recovered and the normal count was soon established. The anemia was attributed entirely to exsanguination by the fleas.

Anemia and even rapidly fatal exsanguination are often observed when rats or other small experimental animals are introduced into a vigorous colony of fleas.

Dermatitis

Some idea of the importance of fleas as pests in the San Francisco Bay area is given by Lunsford (72) who in a paper entitled "Flea Problem in California" quotes the miserable experiences related by early travelers and newcomers. One of the more gifted men of literature wrote of his encounter with fleas, "If any sinning soul ever suffered the punishment of purgatory . . . those torments were endured by myself that night." Some new arrivals were consoled by the prediction that ". . . they would get used to the fleas in time"; thus they were offered a layman's concept of immunity to flea bites, a concept that is now generally accepted. The pest potential of fleas was also admitted by residents of other areas who participated in the dis-

cussion of Lunsford's paper. This writer can only comment that a knowledge of some of the finer points of flea taxonomy in no way mitigates the misery of a dozen or two bites inflicted by Yunnan rat fleas.

The production of desensitizing antigens for flea-bite victims was started in 1939 at the University of California and at the Hooper Foundation for Medical Research. Cherney, Wheeler & Reed (21) desensitized susceptible people with antigens made from fleas collected from dogs. McIvor & Cherney (74, 75) later reared quantities of fleas on laboratory animals for antigen production. Flea antigens were used with "encouraging results" on 128 hypersusceptible people. Follow-up on 82 patients elicited the following responses: 16 reported fewer bites after treatment; 17 stated their reactions were less severe; 43 replied that their bites were not only less severe but fewer in number; five stated they were not benefited; and one child was reported to have aggravated reactions to flea bites following the injections. A major project for study of sensitivity to flea bites is again in progress at the Kaiser Foundation in co-operation with the United States Public Health Service Laboratory in San Francisco.

Our work in public health must be guided by principles such as those expressed, respectively, by the surgeon general of the Public Health Service and by the World Health Organization Constitution (8): "Public health has become more than the absence of disease"; "Health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity." Within these guide lines the pest flea and the pest mosquito must go, along with the plague flea and the malaria mosquito. Presumably the pest-flea problem has been ameliorated by DDT and other modern insecticides, but the writer finds no documentary evidence of this. Flea-bite censuses have not been customary.

Tunga Infestations

There is a special pathological condition, caused by fleas of the genus *Tunga*. This insect is also known as the jigger or chigoe. Jiggers are often confused with "chiggers," which are larval trombiculid mites and quite a different pest. Hopkins & Rothschild (49) recognize six species of *Tunga*, of which only one, *Tunga penetrans* (Linnaeus) is a human parasite.

After fertilization, the female *Tunga* penetrates or firmly attaches to the skin of its host—bird, man, or other mammal—usually on the feet. It is said that the flea burrows, but it is poorly equipped for such action. Somehow the skin envelops the flea except for a small sinus with an external aperture through which eggs and dejecta are passed. This attachment causes intense itching and frequent ulceration as the flea grows to about the size of a small pea. This flea is known in Africa, South America, and adjacent islands.

There is one record of larvae of *Tunga* infesting skin lesions [Faust & Maxwell (33)]. The presence of flea larvae, *Hoplopsyllus glacialis glacialis* (Taschenberg), in the soiled and matted fur of the arctic hare is recorded

by Freeman & Madsen (38). This appears to be normal for the species but is a most unusual habit for flea larvae.

Parasites and Predators of Fleas

One of the first reports of adult fleas parasitized with mites was by Fox (34) who found three rat fleas, *Nosopsyllus fasciatus* (Bosc), so infested. Such mites are observed by nearly everyone who examines large numbers of fleas. Some of the mites, at least, are the hypopial stage of Tyroglyphidae and are merely riders. Some are attached completely exteriorly, and some are found beneath overlapping sclerites. While the mites are not considered to be injurious, a flea so parasitized is often conspicuous for its rough appearance, displaced sclerites, and debris under sclerites. Infestations of 1 to 10 mites per flea are observed and the writer has found them most commonly on rodent fleas of the genus *Opisocrostis*. Sassuchin, Ioff & Tiflow (105) figure another type of mite of the genus *Uropoda* which attaches to fleas by a long posterior stalk, again obviously a rider.

Rothschild & Clay (102), in the popular book *Fleas, Flukes and Cuckoos,* illustrate the mites that infest fleas and credit Leeuwenhoek with the observation that mites prey on larvae of the pigeon flea. They state that this fact inspired the oft-quoted lines by Jonathan Swift, "Big fleas have little fleas upon their back to bite 'em and little fleas have lesser fleas and so ad infinitum." Rothschild & Clay also cite two instances of phoresy in which mallophaga were attached to fleas.

A hymenopterous parasite of tree-squirrel-flea larvae, *Orchopeas wickhami,* in England is reported by Sikes (107) as *Bairamlia fuscipes* Waterston. Numerous small beetles are known to be predatory on fleas [Sassuchin, Ioff & Tiflow (105)].

Miscellaneous Diseases and Microorganisms Associated With Fleas

In addition to the more familiar pathogens which are transmitted by fleas as discussed previously, Steinhaus (113) lists a number of microorganisms that have been associated with fleas in nature or by experiment. Although some of these are potent human pathogens, e.g., the leprosy and glanders bacilli, subsequent experience has failed to show that their flea association is of any epidemiological significance. Others listed are interesting organisms of possible significance to fleas but of no direct importance to human disease. The flea species and their respective microbial associates are as follows:

Ceratophyllus columbae (Walckenaer & Gervais): *Legerella parva* Nöller
Ceratophyllus gallinae (Schrank): *Legerella parva* Nöller
Ceratophyllus sp.: *Herpetomonas pattoni* Swingle
Ctenocephalides canis (Curtis): *Herpetomonas ctenocephali* Mackinnon; *Nosema ctenocephali* Kudo; *Nosema pulicis* Nöller; *Mycobacterium*

leprae (G. A. Hansen) [the leprosy bacillus]; Unidentified organisms

Ctenocephalalides felis (Bouché); *Rickettsia burnetii* Derrick (the organism of Q fever); *Spirochaeta ctenocephali* Patton

Ctenophthalmus agyrtes (Heller): *Crithidia ctenophthalmi* (Mackinnon)

Hystrichopsylla talpae (Curtis): Unidentified "symbiotes"

Leptopsylla segnis (Schönherr): *Herpetomonas ctenopsyllae* Laveran & Franchini

Monopsyllus sciurorum (Schrank) (= *"Ceratophyllus sciurorum"*): *Herpetomonas debreuli* Brumpt

Nosopsyllus fasciatus (Bosc); *Agrippina bona* Strickland; *Legerella grassi* Splendore; Unidentified "symbiotes"

Pulex irritans (Linnaeus): *Diplococcus pneumoniae* Weichselbaum (pneumonia bacillus); *Leptomonas pulicis* Patton & Rao; *Mycobacterium leprae* (G. A. Hansen); *Salmonella choleraesuis* (Smith); Unidentified organisms

Pulex sp.: *Herpetomonas pattoni* Swingle

Xenopsylla cheopis (Rothschild): *Malleomyces pseudomallei* (Whitmore)

Xenopsyllus cleopatrae (Rothschild): *Crithidia cleopatrae*

Flea larvae: *Pseudomoas aeruginosa* (Schroeter); *Salmonella enteritidis* (Gaertner); *Staphylococcus albus* Rosenbach; *Staphylococcus aureus* Rosenbach

In "Materials for the Study of the Parasites and Enemies of Fleas," Sassuchin, Ioff & Tiflow (105) mention many of the microorganisms listed by Steinhaus and, in addition, include: *Malpigiella refringens* Minchin; *Actinocephalus parvus* Wellmer; *Steina rotundata* Ashworth & Rettie; *Gregarina ctenocephalus* Ross.

The role of these organisms as etiologic agents of disease of vertebrates is either unimportant or unknown.

In an extensive paper in Russian on fleas and disease, Ioff (54) gives a table listing 25 diseases associated with fleas. Some of these which have not been discussed in this review are pasteurellosis of chickens, pneumococcus of rodents, staphylococcus of hares, leprosy of rats, bartonellosis of dogs, and anthrax.

Addendum

In the preparation of this review, emphasis has been placed on the earlier, historic aspects of the subject which it seemed useful to assemble with proper citations under one title. Many seemingly trivial observations and references have been cited either because they illustrate some interesting biological principle of disease transmission by fleas or because they would be overlooked in a casual survey of the literature. A publication by Simmons & Hayes (108), "Fleas and Disease," has been of much help.

The serious student of plague cannot miss the important summary papers by Wu (129), Pollitzer (94, 95, 96), Hirst (45), Macchiavello (76), and Swellengrebel (112).

Knowledge gained in the study of fleas and disease has soon been applied to practical control, and, although our information on some of these diseases is still incomplete, the diseases have been controlled. For example, the student of human plague would be hard pressed to find clinical material in this or any country. Endemic and epidemic areas on distribution maps are shrinking. Disease incidence is decreasing. These are rewards each public-health worker can share, no matter how insignificant his own contribution may be.

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